L9 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:682302 CAPLUS
DOCUMENT NUMBER: 129:285991
TITLE: Use of **lactoferrin** in the treatment of **allergen-induced** disorders
INVENTOR(S): Kimber, Ian; Cumberbatch, Marie; Dearman, Rebecca J.; Conneely, Orla M.; Ward, Pauline
PATENT ASSIGNEE(S): Agennix, Inc., USA
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: A61K038-40
CLASSIFICATION: 1-7 (Pharmacology)
Section cross-reference(s): 62, 63
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9844940	A1	19981015	WO 1998-US7234	19980410
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9869647	A1	19981030	AU 1998-69647	19980410
EP 979099	A1	20000216	EP 1998-915471	19980410
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRIORITY APPLN. INFO.:			US 1997-41890	19970410
			WO 1998-US7234	19980410

ABSTRACT:
The present invention relates to pharmaceutical compns. and methods using ***lactoferrin*** for treating allergic disorders characterized by a local immune response including **inflammatory** skin reactions, asthma, and arthritis.

SUPPL. TERM: **lactoferrin** allergen disorder immune response; skin **inflammation** asthma arthritis
lactoferrin
INDEX TERM: Cell migration
(Langerhans' cell; **lactoferrin** in the treatment of **allergen-induced** disorders)
INDEX TERM: UV radiation
(UV-induced **inflammation**; **lactoferrin** in the treatment of **allergen-induced** disorders)
INDEX TERM: Face
(facial skin aging; **lactoferrin** in the treatment of **allergen-induced** disorders)
INDEX TERM: Skin aging

(facial; **lactoferrin** in the treatment of **allergen-induced** disorders)

INDEX TERM: Diapers
Infant
(infant diaper rash; **lactoferrin** in the treatment of **allergen-induced** disorders)

INDEX TERM: Allergy inhibitors
Anti-**inflammatory** drugs
Antiarthritics
Antiasthmatics
Bronchitis
Contact dermatitis
Cosmetics
Dendritic cell
Dermatitis
Drug delivery systems
Keratinocyte
Langerhans' cell
Photoprotectants
Psoriasis
Pulmonary **inflammation**
Rhinitis
Wrinkle-preventing cosmetics
(**lactoferrin** in the treatment of **allergen-induced** disorders)

INDEX TERM: Hydroxy carboxylic acids
ROLE: ADV (Adverse effect, including toxicity); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**lactoferrin** in the treatment of **allergen-induced** disorders)

INDEX TERM: **Interleukin** 1.beta.
ROLE: BAC (Biological activity or effector, except adverse);
BPR (Biological process); BIOL (Biological study); PROC (Process)
(**lactoferrin** in the treatment of **allergen-induced** disorders)

INDEX TERM: **Lactoferrins**
ROLE: BAC (Biological activity or effector, except adverse);
THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**lactoferrin** in the treatment of **allergen-induced** disorders)

INDEX TERM: **Lactoferrin** receptors
Tumor necrosis factor .alpha.
ROLE: BPR (Biological process); BIOL (Biological study); PROC (Process)
(**lactoferrin** in the treatment of **allergen-induced** disorders)

INDEX TERM: Skin diseases
(rash, infant diaper rash; **lactoferrin** in the treatment of **allergen-induced** disorders)

INDEX TERM: Respiratory tract diseases
(sinusitis; **lactoferrin** in the treatment of **allergen-induced** disorders)

INDEX TERM: 302-79-4, Tretinoin
ROLE: ADV (Adverse effect, including toxicity); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**lactoferrin** in the treatment of **allergen-induced** disorders)

=> s interleukin-1?

<------User Break------>
u
SEARCH ENDED BY USER

=> s l5 and l7

L10 119 L5 AND L7

=> s lactoferrin? (w) interleukin?

L11 15 LACTOFERRIN? (W) INTERLEUKIN?

=> s lactoferrin? (s) interleukin?

L12 247 LACTOFERRIN? (S) INTERLEUKIN?

=> s l12 and l7

L13 74 L12 AND L7

=> L13 and allerg?

L13 IS NOT A RECOGNIZED COMMAND
The previous command name entered was not recognized by the system.
For a list of commands available to you in the current file, enter
"HELP COMMANDS" at an arrow prompt (=>).

=> s L13 and allerg?

L14 7 L13 AND ALLERG?

=> d iall 1-7

L14 ANSWER 1 OF 7 MEDLINE
ACCESSION NUMBER: 1998339538 MEDLINE
DOCUMENT NUMBER: 98339538
TITLE: Comparison of **inflammatory** events during developing immunoglobulin E-mediated late-phase reactions and delayed-hypersensitivity reactions.
AUTHOR: Zweiman B; Moskovitz A R; von Allmen C
CORPORATE SOURCE: Department of Medicine, University of Pennsylvania Medical Center, Philadelphia, USA.
CONTRACT NUMBER: RO1 AI 14332 (NIAID)
SOURCE: CLINICAL AND DIAGNOSTIC LABORATORY IMMUNOLOGY, (1998 Jul) 5
(4) 574-7.
Journal code: CB7. ISSN: 1071-412X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199812
ENTRY WEEK: 19981203
ABSTRACT:
To compare cellular and mediator responses in early developing late-phase skin reactions (LPR) and delayed-hypersensitivity (DH) reactions in the same subjects, responses in skin chambers overlying sites of challenge with pollen antigen and Candida albicans antigens were compared in six humans with demonstrated prominent LPR and DH responses. Histamine levels in overlying chamber fluids at 1 h were much higher at LPR than at DH sites (P = 0.002).

After the next 4 h, leukocyte exudation was higher at LPR than at DH sites (P =
0.005). Most leukocytes were activated neutrophils with greater frequency of superoxide-secreting cells and released **lactoferrin** at LPR than at DH sites (P = 0.01 and P = 0.02, respectively). The frequency of exuding eosinophils was higher, but not significantly so (P = 0.5), at LPR sites. Although significantly more eosinophils at LPR sites were activated (P = 0.02),
the levels of released eosinophilic cationic protein were not significantly higher at LPR sites (P = 0.09). The levels of **interleukin**-8 (IL-8),
but not IL-6, were greater at LPR than at DH sites. During the first 5 h of challenge there was greater mast cell activation and subsequent exudation of activated neutrophils at sites of developing LPR than at DH sites, possibly related to greater local IL-8 levels. The frequency of activated eosinophils was also greater at LPR sites. These different initial **inflammatory** responses could play a role in determining expression of LPR or DH reactions.

CONTROLLED TERM: Check Tags: Comparative Study; Human; Support, U.S. Gov't, P.H.S.
Allergens
Candida albicans: IM, immunology
Cytokines: ME, metabolism
Dermatitis, Allergic Contact: ET, etiology
Dermatitis, Allergic Contact: IM, immunology
Diffusion Chambers, Culture
Hay Fever: IM, immunology
Histamine: ME, metabolism
*Hypersensitivity, Delayed: ET, etiology
Hypersensitivity, Delayed: IM, immunology
*IgE: ME, metabolism
***Inflammation: ET, etiology**
Inflammation: IM, immunology
Intradermal Tests
Pollen: IM, immunology
Skin: IM, immunology
Time Factors
CAS REGISTRY NO.: 37341-29-0 (IgE); 51-45-6 (Histamine)
CHEMICAL NAME: 0 (**Allergens**); 0 (Cytokines)

L14 ANSWER 2 OF 7 MEDLINE
ACCESSION NUMBER: 95204853 MEDLINE
DOCUMENT NUMBER: 95204853
TITLE: Products of arachidonic acid metabolism and the effects of cyclooxygenase inhibition on ongoing cutaneous **allergic** reactions in human beings.
AUTHOR: Atkins P C; Zweiman B; Littman B; Presti C; von Allmen C; Moskovitz A; Eskra J D
CORPORATE SOURCE: Department of Medicine, University of Pennsylvania School of Medicine, Philadelphia 19104-6057..
CONTRACT NUMBER: AI-14332 (NIAID)
SOURCE: JOURNAL OF ALLERGY AND CLINICAL IMMUNOLOGY, (1995 Mar) 95 (3) 742-7.
Journal code: H53. ISSN: 0091-6749.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199506
ABSTRACT:
BACKGROUND: There have been conflicting reports about the effects of inhibition
of arachidonic acid metabolism on early- and late-phase cutaneous reactions. We

re-examined this question with a unique nonsteroidal antiinflammatory drug, tenidap sodium. Tenidap sodium has been demonstrated in in vitro studies to inhibit cyclooxygenase, lipoxygenase, and cytokine production (***interleukin*** -1, **interleukin**-6, tumor necrosis factor-alpha). METHODS: In a double-blind, randomized, crossover study, seven pollen-sensitive subjects ingested tenidap (120 mg, by mouth, daily) and placebo for 9 days with a 3-week washout period between treatments. On the eighth day they underwent ***allergen*** skin testing, measurable for up to 12 hours, and on the ninth day they underwent 5-hour skin chamber exposures to **allergen** and buffer. Chamber fluids were analyzed for cellular content, neutrophil granule protein release, cyclooxygenase and lipoxygenase arachidonic acid metabolites, histamine, and tryptase. RESULTS: Tenidap did significantly inhibit cyclooxygenase metabolites at both antigen and buffer sites but had no effect on histamine, tryptase, lipoxygenase metabolites, or granulocyte infiltration. Neutrophil granule release of **lactoferrin** was lower at the antigen site during tenidap administration, but there was no reduction of elastase release. Prostaglandin E2 and leukotriene E4 increased significantly at antigen sites compared with buffer sites during placebo administration and were the most prominent arachidonic acid metabolites detected. CONCLUSION: Tenidap, despite inhibiting cyclooxygenase release at antigen sites, had no effect on skin test responses to antigen or on antigen-induced mediator release or granulocyte infiltration. We conclude that cyclooxygenase metabolites are not important in the development of an **allergic** cutaneous ***inflammatory*** response.

CONTROLLED TERM: Check Tags: Human; Male; Support, U.S. Gov't, P.H.S.
***Anti-Inflammatory Agents, Non-Steroidal: PD, pharmacology**
*Arachidonic Acid: ME, metabolism
Cross-Over Studies
*Cyclooxygenase Inhibitors: PD, pharmacology
Dermatitis, Allergic Contact: IM, immunology
Dermatitis, Allergic Contact: ME, metabolism
***Dermatitis, Allergic Contact: PC, prevention & control**
Double-Blind Method
*Indoles: PD, pharmacology
Skin Tests
CAS REGISTRY NO.: 120210-48-2 (tenidap); 506-32-1 (Arachidonic Acid)
CHEMICAL NAME: 0 (Anti-**Inflammatory** Agents, Non-Steroidal); 0 (Cyclooxygenase Inhibitors); 0 (Indoles)

L14 ANSWER 3 OF 7 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:682302 CAPLUS
DOCUMENT NUMBER: 129:285991
TITLE: Use of lactoferrin in the treatment of **allergen**-induced disorders
INVENTOR(S): Kimber, Ian; Cumberbatch, Marie; Dearman, Rebecca J.; Conneely, Orla M.; Ward, Pauline
PATENT ASSIGNEE(S): Agennix, Inc., USA
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: A61K038-40
CLASSIFICATION: 1-7 (Pharmacology)
Section cross-reference(s): 62, 63
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9844940	A1	19981015	WO 1998-US7234	19980410
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9869647	A1	19981030	AU 1998-69647	19980410
EP 979099	A1	20000216	EP 1998-915471	19980410
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRIORITY APPLN. INFO.:			US 1997-41890	19970410
			WO 1998-US7234	19980410

ABSTRACT:
The present invention relates to pharmaceutical compns. and methods using lactoferrin for treating **allergic** disorders characterized by a local immune response including **inflammatory** skin reactions, asthma, and arthritis.

SUPPL. TERM: lactoferrin **allergen** disorder immune response; skin **inflammation** asthma arthritis lactoferrin

INDEX TERM: Cell migration
(Langerhans' cell; lactoferrin in the treatment of **allergen**-induced disorders)

INDEX TERM: UV radiation
(UV-induced **inflammation**; lactoferrin in the treatment of **allergen**-induced disorders)

INDEX TERM: Face
(facial skin aging; lactoferrin in the treatment of **allergen**-induced disorders)

INDEX TERM: Skin aging
(facial; lactoferrin in the treatment of **allergen**-induced disorders)

INDEX TERM: Diapers
Infant
(infant diaper rash; lactoferrin in the treatment of **allergen**-induced disorders)

INDEX TERM: **Allergy** inhibitors
Anti-**inflammatory** drugs
Antiarthritics
Antiasthmatics
Bronchitis
Contact dermatitis
Cosmetics
Dendritic cell
Dermatitis
Drug delivery systems
Keratinocyte
Langerhans' cell
Photoprotectants
Psoriasis
Pulmonary **inflammation**
Rhinitis
Wrinkle-preventing cosmetics
(lactoferrin in the treatment of **allergen**-induced disorders)

INDEX TERM: Hydroxy carboxylic acids
ROLE: ADV (Adverse effect, including toxicity); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lactoferrin in the treatment of **allergen**-induced disorders)

INDEX TERM: **Interleukin** 1.beta.
ROLE: BAC (Biological activity or effector, except adverse);
BPR (Biological process); BIOL (Biological study); PROC (Process)
(**lactoferrin** in the treatment of **allergen**-induced disorders)
INDEX TERM: Lactoferrins
ROLE: BAC (Biological activity or effector, except adverse);
THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lactoferrin in the treatment of **allergen**-induced disorders)
INDEX TERM: Lactoferrin receptors
Tumor necrosis factor .alpha.
ROLE: BPR (Biological process); BIOL (Biological study); PROC (Process)
(lactoferrin in the treatment of **allergen**-induced disorders)
INDEX TERM: Skin diseases
(rash, infant diaper rash; lactoferrin in the treatment of **allergen**-induced disorders)
INDEX TERM: Respiratory tract diseases
(sinusitis; lactoferrin in the treatment of **allergen**-induced disorders)
INDEX TERM: 302-79-4, Tretinoin
ROLE: ADV (Adverse effect, including toxicity); BUU (Biological use, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(lactoferrin in the treatment of **allergen**-induced disorders)

L14 ANSWER 4 OF 7 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1995:359728 CAPLUS
DOCUMENT NUMBER: 122:130898
TITLE: Lactoferrin inhibits the effector phase of the delayed type hypersensitivity to sheep erythrocytes and **inflammatory** reactions to M. bovis (BCG)
AUTHOR(S): Zimecki, Michal; Machnicki, Michal
CORPORATE SOURCE: Institute Immunology and Experimental Therapy, Polish Academy Sciences, Wroclaw, 53-114, Pol.
SOURCE: Arch. Immunol. Ther. Exp. (1994), 42(3), 171-7
CODEN: AITEAT; ISSN: 0004-069X
DOCUMENT TYPE: Journal
LANGUAGE: English
CLASSIFICATION: 15-9 (Immunochemistry)
ABSTRACT:
Bovine lactoferrin (BLF) given to mice, sensitized to SRBC, together with the eliciting dose of antigen, inhibits very strongly the DTH reaction measured after 24 h by foot pad swelling. Administration of BLF at 48 or 24 h before eliciting the DTH reaction was not effective, however, BLF suppressed the reaction when given at the peak of the **inflammatory** process. The effects of BLF were strongest when the protein was injected i.v. I.p. or i.m. administrations of BLF were less inhibitory. In addn., BLF diminishes, although to a much lesser degree, the **inflammatory** reactions induced by BCG. The inhibitory action of BLF does not involve liver since treatment of mice with galactosamine does not reverse the inhibition. Studies on cytokine prodn. revealed that peritoneal macrophages, derived from mice pretreated with LF, have an increased ability to produce in vitro IL-6 after induction with LPS. In addn., we demonstrated that inhibition of macrophage migration, mediated by migration inhibition factor, is abolished by BLF. Lastly, the inhibitory effect of BLF could not be transferred with serum from donors treated with BLF. In summary, the data reveal the inhibitory properties of LF,

administered systematically, in relation to locally induced ***inflammation*** .

SUPPL. TERM: lactoferrin delayed type hypersensitivity erythrocyte; **inflammation** Mycobacterium macrophage **interleukin lactoferrin**

INDEX TERM: Erythrocyte
Inflammation
Mycobacterium BCG
(lactoferrin inhibits the effector phase of the delayed type hypersensitivity to sheep erythrocytes and **inflammatory** reactions to M. bovis (BCG))

INDEX TERM: Lactoferrins
ROLE: BAC (Biological activity or effector, except adverse);
BIOL (Biological study)
(lactoferrin inhibits the effector phase of the delayed type hypersensitivity to sheep erythrocytes and **inflammatory** reactions to M. bovis (BCG))

INDEX TERM: Macrophage
(macrophages pretreated with lactoferrin have increased ability to produce IL-6 after induction with LPS)

INDEX TERM: Lipopolysaccharides
ROLE: BAC (Biological activity or effector, except adverse);
BIOL (Biological study)
(macrophages pretreated with lactoferrin have increased ability to produce IL-6 after induction with LPS)

INDEX TERM: **Allergy**
(delayed hypersensitivity, lactoferrin inhibits the effector phase of the delayed type hypersensitivity to sheep erythrocytes and **inflammatory** reactions to M. bovis (BCG))

INDEX TERM: Lymphokines and Cytokines
ROLE: MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)
(**interleukin** 6, macrophages pretreated with **lactoferrin** have increased ability to produce IL-6 after induction with LPS)

L14 ANSWER 5 OF 7 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1998:363166 BIOSIS
DOCUMENT NUMBER: PREV199800363166
TITLE: Comparison of **inflammatory** events during developing immunoglobulin E-mediated late-phase reactions and delayed-hypersensitivity reactions.
AUTHOR(S): Zweiman, Burton (1); Moskovitz, Anne R.; Von Allmen, Carolyn
CORPORATE SOURCE: (1) Univ. Pennsylvania Sch. Med., 512 Johnson Pavilion, Philadelphia, PA 19104-6057 USA
SOURCE: Clinical and Diagnostic Laboratory Immunology, (July, 1998)
Vol. 5, No. 4, pp. 574-577.
ISSN: 1071-412X.
DOCUMENT TYPE: Article
LANGUAGE: English
ABSTRACT:
To compare cellular and mediator responses in early developing late-phase skin reactions (LPR) and delayed-hypersensitivity (DH) reactions in the same subjects, responses in skin chambers overlying sites of challenge with pollen antigen and Candida albicans antigens were compared in six humans with demonstrated prominent LPR and DH responses. Histamine levels in overlying chamber fluids at 1 h were much higher at LPR than at DH sites (P = 0.002). After the next 4 h, leukocyte exudation was higher at LPR than at DH sites (P =

0.005). Most leukocytes were activated neutrophils with greater frequency of superoxide-secreting cells and released **lactoferrin** at LPR than at DH sites (P = 0.01 and P = 0.02, respectively). The frequency of exuding eosinophils was higher, but not significantly so (P = 0.5), at LPR sites. Although significantly more eosinophils at LPR sites were activated (P = 0.02),
the levels of released eosinophilic cationic protein were not significantly higher at LPR sites (P = 0.09). The levels of **interleukin**-8 (IL-8), but not IL-6, were greater at LPR than at DH sites. During the first 5 h of challenge there was greater mast cell activation and subsequent exudation of activated neutrophils at sites of developing LPR than at DH sites, possibly related to greater local IL-8 levels. The frequency of activated eosinophils was also greater at LPR sites. These different initial **inflammatory** responses could play a role in determining expression of LPR or DH reactions.

CONCEPT CODE: Immunology and Immunochemistry - Immunopathology, Tissue Immunology *34508
Cytology and Cytochemistry - Human *02508
Biochemical Studies - Proteins, Peptides and Amino Acids *10064
Biophysics - Molecular Properties and Macromolecules *10506
Pathology, General and Miscellaneous - Inflammation and Inflammatory Disease *12508
Blood, Blood-Forming Organs and Body Fluids - Lymphatic Tissue and Reticuloendothelial System *15008
Endocrine System - General *17002
Integumentary System - Pathology *18506
Allergy *35500

BIOSYSTEMATIC CODE: Hominidae 86215

INDEX TERMS: Major Concepts
Clinical Immunology (Human Medicine, Medical Sciences)

INDEX TERMS: Parts, Structures, & Systems of Organisms
activated neutrophils; eosinophilic cationic protein; eosinophils: blood and lymphatics, immune system; mast cells: activation, immune system; superoxide-secreting cells

INDEX TERMS: Diseases
delayed-hypersensitivity reaction: immune system disease; late-phase skin reactions: immune system disease, integumentary system disease

INDEX TERMS: Chemicals & Biochemicals
histamine; lactoferrin; pollen antigen: **allergen**; Candida-albicans antigen; IL-6 [interleukin-6]; IL-8 [interleukin-8]

INDEX TERMS: Miscellaneous Descriptors
inflammation

ORGANISM: Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia

ORGANISM: Organism Name
human (Hominidae): patient

ORGANISM: Organism Superterms
Animals; Chordates; Humans; Mammals; Primates; Vertebrates

REGISTRY NUMBER: 51-45-6 (HISTAMINE)
11062-77-4 (SUPEROXIDE)

L14 ANSWER 6 OF 7 BIOSIS COPYRIGHT 2000 BIOSIS

ACCESSION NUMBER: 1995:201372 BIOSIS

DOCUMENT NUMBER: PREV199598215672

TITLE: Products of arachidonic acid metabolism and the effects of cyclooxygenase inhibition on ongoing cutaneous **allergic** reactions in human beings.

AUTHOR(S): Atkins, Paul C. (1); Zweiman, Burton; Littman, Bruce; Presti, Charles; Von Allmen, Carolyn; Moskovitz, Anne; Eskra, J. D.

CORPORATE SOURCE: (1) 510 Johnson Pavilion, Univ. Pennsylvania Sch. Med., Philadelphia, PA 19104-6057 USA
SOURCE: Journal of Allergy and Clinical Immunology, (1995) Vol. 95,
No. 3, pp. 742-747.
ISSN: 0091-6749.
DOCUMENT TYPE: Article
LANGUAGE: English
ABSTRACT:
Background: There have been conflicting reports about the effects of inhibition of arachidonic acid metabolism on early- and late-phase cutaneous reactions. We reexamined this question with a unique nonsteroidal antiinflammatory drug, tenidap sodium. Tenidap sodium has been demonstrated in in vitro studies to inhibit cyclooxygenase, lipoxygenase, and cytokine production (***interleukin*** -1, **interleukin**-6, tumor necrosis factor-alpha). Methods: In a double-blind, randomized, crossover study, seven pollen-sensitive subjects ingested tenidap (120 mg, by mouth, daily) and placebo for 9 days with a 3-week washout period between treatments. On the eighth day they underwent ***allergen*** skin testing, measurable for up to 12 hours, and on the ninth day they underwent 5-hour skin chamber exposures to **allergen** and buffer. Chamber fluids were analyzed for cellular content, neutrophil granule protein release, cyclooxygenase and lipoxygenase arachidonic acid metabolites, histamine, and tryptase. Results: Tenidap did significantly inhibit cyclooxygenase metabolites at both antigen and buffer sites but had no effect on histamine, tryptase, lipoxygenase metabolites, or granulocyte infiltration. Neutrophil granule release of **lactoferrin** was lower at the antigen site during tenidap administration, but there was no reduction of elastase release. Prostaglandin E-2 and leukotriene E-4 increased significantly at antigen sites compared with buffer sites during placebo administration and were the most prominent arachidonic acid metabolites detected. Conclusion: Tenidap, despite inhibiting cyclooxygenase release at antigen sites, had no effect on skin test responses to antigen or on antigen-induced mediator release or granulocyte infiltration. We conclude that cyclooxygenase metabolites are not important in the development of an **allergic** cutaneous ***inflammatory*** response.
CONCEPT CODE: Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Biochemical Studies - Lipids 10066
Enzymes - Physiological Studies *10808
Pathology, General and Miscellaneous - Inflammation and Inflammatory Disease *12508
Metabolism - Lipids *13006
Blood, Blood-Forming Organs and Body Fluids - Lymphatic Tissue and Reticuloendothelial System *15008
Endocrine System - General *17002
Integumentary System - Pathology *18506
Immunology and Immunochemistry - Immunopathology, Tissue Immunology *34508
Allergy *35500
BIOSYSTEMATIC CODE: Hominidae *86215
INDEX TERMS: Major Concepts
Allergy (Clinical Immunology, Human Medicine, Medical Sciences); Blood and Lymphatics (Transport and Circulation); Clinical Immunology (Human Medicine, Medical Sciences); Dermatology (Human Medicine, Medical Sciences); Endocrine System (Chemical Coordination and Homeostasis); Enzymology (Biochemistry and Molecular Biophysics); Metabolism; Pathology
INDEX TERMS: Chemicals & Biochemicals
ARACHIDONIC ACID; CYCLOOXYGENASE; LEUKOTRIENE E4

INDEX TERMS: Miscellaneous Descriptors
LEUKOTRIENE E4; PROSTAGLANDIN E2
ORGANISM: Super Taxa
Hominidae: Primates, Mammalia, Vertebrata, Chordata, Animalia
ORGANISM: Organism Name
Hominidae (Hominidae)
ORGANISM: Organism Superterms
animals; chordates; humans; mammals; primates; vertebrates
REGISTRY NUMBER: 506-32-1 (ARACHIDONIC ACID)
39391-18-9 (CYCLOOXYGENASE)
75715-89-8 (LEUKOTRIENE E4)

L14 ANSWER 7 OF 7 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1991:287599 BIOSIS
DOCUMENT NUMBER: BR41:8019
TITLE: MODULATION OF PHENOTYPIC AND FUNCTIONAL PROPERTIES OF HUMAN
MONOCYTES BY **INTERLEUKIN**-4 AND BOVINE **LACTOFERRIN**.
AUTHOR(S): PAUL-EUGENE N; DUGAS B; LAGENTE V; CHOUAIB S; MENCIA-HUERTA
J M; GALLACIER J P; BRAQUET P; RIALLAND J P; PAUBERT-BRAQUET M
CORPORATE SOURCE: INSTITUT HENRI BEAUFOUR, 91952 LES ULIS, FR.
SOURCE: 75TH ANNUAL MEETING OF THE FEDERATION OF AMERICAN SOCIETIES
FOR EXPERIMENTAL BIOLOGY, ATLANTA, GEORGIA, USA, APRIL 21-25, 1991. FASEB (FED AM SOC EXP BIOL) J, (1991) 5 (5), A1012.
CODEN: FAJOEC. ISSN: 0892-6638.
DOCUMENT TYPE: Conference
FILE SEGMENT: BR; OLD
LANGUAGE: English
CONCEPT CODE: General Biology - Symposia, Transactions and Proceedings of
Conferences, Congresses, Review Annuals 00520
Cytology and Cytochemistry - Human *02508
Biochemical Studies - Proteins, Peptides and Amino Acids 10064
Pathology, General and Miscellaneous - Inflammation and Inflammatory Disease *12508
Blood, Blood-Forming Organs and Body Fluids - Blood Cell Studies *15004
Blood, Blood-Forming Organs and Body Fluids - Lymphatic Tissue and Reticuloendothelial System *15008
Immunology and Immunochemistry - Immunopathology, Tissue Immunology *34508
Allergy 35500
BIOSYSTEMATIC CODE: Bovidae 85715
Hominidae 86215
INDEX TERMS: Miscellaneous Descriptors
ABSTRACT HUMAN **ALLERGY INFLAMMATION**

=> duplicate remove

ENTER L# LIST OR (END):L5

DUPLICATE IS NOT AVAILABLE IN 'CAOLD'.
ANSWERS FROM THESE FILES WILL BE CONSIDERED UNIQUE
DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n

PROCESSING COMPLETED FOR L5

L15 217 DUPLICATE REMOVE L5 (167 DUPLICATES REMOVED)

=> s l15 and (lactoferrin? (p) interleukin?)

PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'TOFERRIN? (P) INTERLEUK'
L16 149 L15 AND (LACTOFERRIN? (P) INTERLEUKIN?)

=> s l15 and (pharmaceuti? or therapeuti?)

L17 20 L15 AND (PHARMACEUTI? OR THERAPEUTI?)

=> d ibib abs 1-5

L17 ANSWER 1 OF 20 MEDLINE
ACCESSION NUMBER: 1999003149 MEDLINE
DOCUMENT NUMBER: 99003149
TITLE: Complement activation in relation to capillary leakage in children with septic shock and purpura.
AUTHOR: Hazelzet J A; de Groot R; van Mierlo G; Joosten K F; van der Voort E; Eerenberg A; Suur M H; Hop W C; Hack C E
CORPORATE SOURCE: Divisions of Pediatric Intensive Care, Department of Pediatrics, Sophia Children's Hospital/University Hospital Rotterdam, The Netherlands.. hazelzet@alg.azr.nl
SOURCE: INFECTION AND IMMUNITY, (1998 Nov) 66 (11) 5350-6. Journal code: GO7. ISSN: 0019-9567.
PUB. COUNTRY: United States
(CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199901
ENTRY WEEK: 19990104
AB To assess the relationship between capillary leakage and inflammatory mediators during sepsis, blood samples were taken on hospital admission, as well as 24 and 72 h later, from 52 children (median age, 3.3 years) with severe meningococcal sepsis, of whom 38 survived and 14 died. Parameters related to cytokines (**interleukin** 6 [IL-6] IL-8, plasma phospholipase A2, and C-reactive protein [CRP]), to neutrophil degranulation (elastase and **lactoferrin**), to complement activation (C3a, C3b/c, C4b/c, and C3- and C4-CRP complexes), and to complement regulation (functional and inactivated C1 inhibitor and C4BP) were determined. The degree of capillary leakage was derived from the amount of plasma infused and the severity of disease by assessing the pediatric risk of mortality (PRISM) score. Levels of IL-6, IL-8, C3b/c, C3-CRP complexes, and C4BP on admission, adjusted for the duration of skin lesions, were significantly different in survivors and nonsurvivors (C3b/c levels were on average 2.2 times higher in nonsurvivors, and C3-CRP levels were 1.9 times higher in survivors). Mortality was independently related to the levels of C3b/c and C3-CRP complexes. In agreement with this, levels of complement activation products correlated well with the PRISM score or capillary leakage. Thus, these data show that complement activation in patients with severe meningococcal sepsis is associated with a poor outcome and a more severe disease course. Further studies should reveal whether complement activation may be a target for **therapeutical** intervention in this disease.

L17 ANSWER 2 OF 20 MEDLINE
ACCESSION NUMBER: 1998273763 MEDLINE

DOCUMENT NUMBER: 98273763
TITLE: **Lactoferrin** lowers serum **interleukin** 6 and tumor necrosis factor alpha levels in mice subjected to surgery.
AUTHOR: Zimecki M; Wlaszczyk A; Zagulski T; Kubler A
CORPORATE SOURCE: Institute of Immunology and Experimental Therapy, Polish Academy of Sciences, Wroclaw.
SOURCE: ARCHIVUM IMMUNOLOGIAE ET THERAPIAE EXPERIMENTALIS, (1998) 46 (2) 97-104.
Journal code: 79O. ISSN: 0004-069X.
PUB. COUNTRY: Poland
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199810
ENTRY WEEK: 19981002

AB Mice subjected to thymectomy or splenectomy in general anesthesia release **interleukin** 6 (IL-6) and tumor necrosis factor alpha (TNF-alpha) into circulation reaching high concentrations after 4 h following operation. In the case of thymectomy IL-6 can be detected only on the day of operation and TNF-alpha attains a maximal value on day 3 postoperation.

Splenectomy, which is a more extensive surgical operation, results in a higher, and more prolonged existence of IL-6 in circulation accompanied by higher levels of TNF-alpha. Bovine **lactoferrin** (BLF; 10 mg/mouse), given intravenously (i.v.) 24 h before thymectomy, reduced, on average, the level of serum IL-6 by 70% as measured 4 h after operation. The inhibiting effect of BLF on TNF-alpha production was smaller with a mean 30% reduction. The effects of BLF (i.v.) administration on the cytokine levels following splenectomy were less inhibitory. BLF caused an approximate 35% fall in IL-6 levels and even weaker effects (20% inhibition) on TNF-alpha release. Application of much lower (1-0.2 mg) per os doses of BLF was even more effective in lowering IL-6 levels after thymectomy (up to 90%) after 5 BLF doses, and by 55% of TNF-alpha. The data suggest that **lactoferrin** may find **therapeutical** application for diminishing manifestations of shock caused by clinical insults.

L17 ANSWER 3 OF 20 MEDLINE
ACCESSION NUMBER: 1998168225 MEDLINE
DOCUMENT NUMBER: 98168225
TITLE: Functional studies of maturing myeloid cells during ex vivo expansion for treatment of aplasia: feasibility of ex vivo expansion from cryopreserved bone marrow cell samples.
AUTHOR: Neildez-Nguyen T M; Vetillard J; Drouet M; Herodin F; Brouard N; Mestries J C; Thierry D
CORPORATE SOURCE: Institut de Protection et de Surete Nucleaire, Departement de Protection de la sante de I'Homme et de Dosimetrie, Fontenay-aux-Roses, France.
SOURCE: JOURNAL OF HEMATOTHERAPY, (1998 Feb) 7 (1) 69-79.
Journal code: B3T. ISSN: 1061-6128.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199808
ENTRY WEEK: 19980801

AB Ex vivo expanded CD34+ progenitor cells from fresh or cryopreserved primate bone marrow, induced to granulocytic differentiation with growth factors, were investigated to determine whether myeloid cells produced in liquid cultures have the normal biologic functions needed for the

treatment of patients with neutropenia following high-dose chemotherapy or **therapeutic** or accidental radiation exposure. Human and simian (baboons or macaques) CD34+ cells were cultured with granulocyte-colony stimulating factor (G-CSF), stem cell factor (SCF), **interleukin** -1 (IL-1), IL-3, and IL-6, and assessed at 14 days of culture for their capacity to respond to different functional tests. Immunostaining revealed that human ex vivo expanded cells contained myeloperoxydase (MPO, 82% +/- 8%) and **lactoferrin** (LF, 30% +/- 6%) in their granules. Maturation of cultured cells was associated with stimulated chemotactic responsiveness and respiratory burst activity (superoxide anion and hydrogen peroxide production) in expansions from human, baboon, and macaque CD34+ progenitor cells. Mature cells obtained from ex vivo expansion of selected cryopreserved human bone marrow CD34+ cells presented reduced but significant functional activities (chemotactic responsiveness and hydrogen peroxide production) when compared with human peripheral blood neutrophils. The validation of nonhuman primate ex vivo expansion systems may permit their use as models of irradiation. The feasibility of ex vivo expansion from cryopreserved bone marrow cell samples may offer considerable opportunity for banking bone marrow for autologous transfusion.

L17 ANSWER 4 OF 20 MEDLINE
ACCESSION NUMBER: 97413344 MEDLINE
DOCUMENT NUMBER: 97413344
TITLE: Modulation of cytokine release and neutrophil function by granulocyte colony-stimulating factor during endotoxemia in humans.
AUTHOR: Pajkrt D; Manten A; van der Poll T; Tiel-van Buul M M; Jansen J; Wouter ten Cate J; van Deventer S J
CORPORATE SOURCE: Department of Nuclear Medicine, and Center for Hemostasis, Thrombosis, Atherosclerosis and Inflammation Research, Academic Medical Center, University of Amsterdam, The Netherlands.
SOURCE: BLOOD, (1997 Aug 15) 90 (4) 1415-24.
Journal code: A8G. ISSN: 0006-4971.
PUB. COUNTRY: United States
(CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals
ENTRY MONTH: 199711
ENTRY WEEK: 19971104
AB In this double-blind, cross-over, placebo-controlled, randomized study, two groups of eight healthy male volunteers were challenged with endotoxin (4 ng/kg) on two occasions, once in conjunction with placebo and once with granulocyte colony-stimulating factor (G-CSF; 5 microg/kg). In group 1, G-CSF was administered intravenously 2 hours before endotoxin challenge; in group 2, G-CSF was administered subcutaneously 24 hours before endotoxin challenge. In group 1, G-CSF significantly enhanced the release of tumor necrosis factor (TNF), **interleukin**-6 (IL-6), IL-8, IL-1 receptor antagonist (IL-1ra), and soluble TNF receptors. In group 2, G-CSF significantly reduced IL-8 concentrations and modestly attenuated TNF and IL-6 levels. In this group, IL-1ra and soluble TNF receptors were enhanced by G-CSF pretreatment and lipopolysaccharide (LPS)-induced soluble TNF receptor release was further augmented, whereas LPS-induced IL-1ra concentrations remained unaltered. Both pretreatments with G-CSF increased

LPS-induced peripheral neutrophilia; the expression of CD11b, CD18, and CD67; and the release of elastase and **lactoferrin**. Both pretreatments also down-regulated neutrophil L-selectin expression and prevented the endotoxin-induced pulmonary neutrophil accumulation during the first 2 hours after endotoxin challenge. These data indicate that two different pretreatments with G-CSF result in differential effects on LPS-induced cytokine release but similar effects on LPS-induced neutrophil activation and changes in expression of cell surface molecules. Finally, regardless of the effects of G-CSF on LPS-induced cytokine release, G-CSF blocks LPS-induced pulmonary granulocyte accumulation.

L17 ANSWER 5 OF 20 MEDLINE
ACCESSION NUMBER: 97320669 MEDLINE
DOCUMENT NUMBER: 97320669
TITLE: Relation of **lactoferrin** levels in gastric mucosa with Helicobacter pylori infection and with the degree of gastric inflammation.
AUTHOR: Nakao K; Imoto I; Ikemura N; Shibata T; Takaji S; Taguchi Y; Misaki M; Yamauchi K; Yamazaki N
CORPORATE SOURCE: Third Department of Internal Medicine, Mie University School of Medicine, the National Tsu Hospital, Japan.
SOURCE: AMERICAN JOURNAL OF GASTROENTEROLOGY, (1997 Jun) 92 (6) 1005-11.
Journal code: 3HE. ISSN: 0002-9270.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199709
ENTRY WEEK: 19970902
AB OBJECTIVES: **Lactoferrin** (Lf) is an iron-binding glycoprotein present in milk, lacrimae, saliva, and gastroduodenal secretions. In vitro studies disclosed contradicting results regarding the relation of Lf with Helicobacter pylori (HP) infection. This study aimed to investigate the relationship between the gastric mucosal concentration of Lf and HP infection of the stomach. The relationship of the gastric mucosal level of Lf with the gastric mucosal concentration of **interleukin**-8 (IL-8) and with the intragastric ammonia levels was also assessed. In addition, the gastric mucosal Lf levels before and after irradication of HP infection were also evaluated. METHODS: This study was composed of 27 HP-positive and 12 HP-negative patients with chronic gastritis. Gastric mucosal biopsy specimens were obtained from all subjects by endoscopy, and the degree of histological inflammatory changes were assessed according to the Sydney system. The gastric mucosal levels of Lf and IL-8 were measured by immunoassays. Assessment of the effect of therapy on the gastric mucosal level of Lf was performed in 10 patients with HP-associated duodenal ulcer. RESULTS: Lf, IL-8, and ammonia levels were significantly higher in patients with HP-positive gastritis compared with those with HP-negative gastritis in both the antrum and the gastric body. Histologically, the degree of inflammatory changes correlated significantly with the Lf levels in the gastric mucosa. Furthermore, the degree of HP colonization was more significant in biopsy samples from the antrum than in those from the corpus of the stomach. The gastric mucosal levels of Lf and IL-8 correlated significantly in the antrum and the gastric body. The ammonia intragastric level significantly correlated with the mucosal Lf level in the antrum and in the gastric body. Therapy significantly decreased the Lf levels in the gastric mucosa of the antrum ($p < 0.005$) and the gastric body ($p < 0.005$). CONCLUSION: The results of

the present investigation showed, for the first time in vivo, that Lf concentration is increased in the biopsy specimens of patients with HP-related gastritis, and that the levels of Lf correlate significantly with the degree of inflammation of the gastric mucosa. The gastric mucosal level of Lf may constitute an excellent marker of HP infection.

=> d ibib abs 6-20

L17 ANSWER 6 OF 20 MEDLINE
ACCESSION NUMBER: 96437021 MEDLINE
DOCUMENT NUMBER: 96437021
TITLE: Effects of recombinant soluble type I **interleukin** -1 receptor on human inflammatory responses to endotoxin.
AUTHOR: Preas H L 2nd; Reda D; Tropea M; Vandivier R W; Banks S M; Agosti J M; Suffredini A F
CORPORATE SOURCE: Critical Care Medicine Department, Warren G. Magnuson Clinical Center, National Institutes of Health, Bethesda, MD 20892-1662, USA.
SOURCE: BLOOD, (1996 Oct 1) 88 (7) 2465-72.
Journal code: A8G. ISSN: 0006-4971.
PUB. COUNTRY: United States
(CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals
ENTRY MONTH: 199701
ENTRY WEEK: 19970104
AB Effects of soluble recombinant human type I **interleukin**-1 receptor (sIL-1RI) were evaluated in 18 volunteers given intravenous endotoxin and randomized to placebo (n = 6), low-dose (n = 6), or high-dose (n = 6) sIL-1RI. Soluble IL-1RI decreased IL-1 beta (P = .001), but decreased IL-1ra (P = .0001), and resulted in 10-fold and 43-fold dose-related increases in sIL-1RI-IL-1ra complexes compared with placebo (P < or = .001). High-dose sIL-1RI was associated with increased levels of immunoactive tumor necrosis factor-alpha (P = .02), IL-8 (P = .0001), and cell-associated IL-1 beta (P = .047). C-reactive protein levels were higher after sIL-1RI than placebo (P = .035). Soluble IL-1RI decreased the severity of chills (P = .03), but did not alter other symptoms, changes in temperature, systemic hemodynamic responses, or changes in leukocyte and platelet number. Thus, sIL-1RI had no discernable antiinflammatory effect following endotoxin administration due in part to low levels of circulating IL-1 beta and neutralization of IL-1ra inhibitory function. This latter interaction represents an indirect mechanism of agonist activity elicited by sIL-1RI and may contribute to increases in inflammatory mediators, limiting therapy with sIL-1RI during endotoxemia.

L17 ANSWER 7 OF 20 MEDLINE
ACCESSION NUMBER: 96108886 MEDLINE
DOCUMENT NUMBER: 96108886
TITLE: IL-1 beta does not cause neutrophil degranulation but does lead to IL-6, IL-8, and nitrite/nitrate release when used in patients with cancer.
AUTHOR: Ogilvie A C; Hack C E; Wagstaff J; van Mierlo G J; Erenberg A J; Thomsen L L; Hoekman K; Rankin E M
CORPORATE SOURCE: Department of Medical Oncology, The Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital, University of

Amsterdam.
SOURCE: JOURNAL OF IMMUNOLOGY, (1996 Jan 1) 156 (1) 389-94.
Journal code: IFB. ISSN: 0022-1767.
PUB. COUNTRY: United States
(CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE I)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals; Cancer Journals
ENTRY MONTH: 199606
AB The use of IL-1 in humans is associated with dose-limiting toxicity which resembles that of TNF-alpha or IL-2. Activation of neutrophils is thought to contribute to the toxicity caused by these two cytokines. We studied the effect of IL-1 in vivo on changes in neutrophil numbers and neutrophil degranulation as well as on the formation of neutrophil agonists, such as complement activation products, and on levels of TNF, IL-6, IL-8, and nitrite/nitrate (as a measure of nitric oxide production). Six patients with metastatic melanoma were treated with 3 ng/kg recombinant human IL-1 beta daily. One hour after the start of the 30-min IL-1 infusion, which caused mild cardiovascular toxicity, plasma levels of IL-6 reached a peak of 25 +/- 9 ng/L (mean +/- SEM), IL-8 reached a peak of 311 +/- 100 ng/L at 2 h, and nitrite/nitrate peaked after 10 h to 89 +/- 27 mumol/L. IL-1 did not induce significant changes in plasma levels of TNF or of the complement activation products C3a and C4b/c. Although IL-1 induced neutrophilia, levels of elastase and **lactoferrin** did not change. The failure of IL-1 to degranulate neutrophils was confirmed in an ex vivo model with whole blood culture in which doses of up to 100 microgram/L IL-1 beta or IL-1 alpha failed to induce significant elastase or **lactoferrin** release, whereas TNF, tested as a positive control, was able to do so. These results demonstrate that, unlike TNF, IL-1 does not cause neutrophil degranulation in man, despite its ability to cause neutrophilia and the rapid release of IL-6, IL-8, and nitrite/nitrate.

L17 ANSWER 8 OF 20 MEDLINE
ACCESSION NUMBER: 95210148 MEDLINE
DOCUMENT NUMBER: 95210148
TITLE: The release of **interleukin**-8 during intravenous bolus treatment with **interleukin**-2.
AUTHOR: Baars J W; Wolbink G J; Hart M H; Hack C E; Eerenberg-Belmer A J; Pinedo H M; Wagstaff J
CORPORATE SOURCE: Department of Medical Oncology, Free University Hospital, Amsterdam, The Netherlands.
SOURCE: ANNALS OF ONCOLOGY, (1994 Dec) 5 (10) 929-34.
Journal code: AYF. ISSN: 0923-7534.
PUB. COUNTRY: Netherlands
(CLINICAL TRIAL)
(CLINICAL TRIAL, PHASE II)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199507
AB OBJECTIVE: To study the role that **interleukin**-8 might play in the activation of polymorphonuclear neutrophils during **interleukin**-2 therapy and the relationship of these phenomena to **interleukin**-2 induced toxicity. DESIGN: A cohort study with measurements before and after the administration of **interleukin**-2. SETTING: Medical oncology department of a large teaching hospital. PATIENTS: Fourteen patients with metastatic renal cell carcinoma and 10 with metastatic melanoma being treated in a phase 2 study of the sequential combination of interferon-gamma and **interleukin**-2. MEASUREMENTS: Plasma levels of tumour necrosis factor-alpha, **interleukins**-6 and 8 and

markers of neutrophil activation (neutrophil elastase and **lactoferrin**) were measured in patients receiving 5 daily injections of interferon-gamma (100 micrograms/m2/day) followed by 5 days of **interleukin**-2 (18 x 10(6) IU/m2/day). MAIN RESULTS: Tumour necrosis factor-alpha rose from baseline levels of 32 (range, 12 to 56) to 343 (103 to 787) pg/ml 3 hours after **interleukin**-2 administration returning to baseline values 21 hours later. **Interleukins**-6 and -8 rose from baseline levels of 6 (5 to 10) and 75 (35 to 100) to 2151 (152 to 7259) and 1283 (490 to 2500) pg/ml, respectively, at 4 hours after **interleukin**-2 with both returning to baseline values by 24 hours. Peak levels of neutrophil elastase and **lactoferrin**, both markers of neutrophil activation, occurred 6 hours after **interleukin**-2 administration. CONCLUSIONS: These data indicate that following administration of **interleukin**-2 tumour necrosis factor-alpha is released followed sequentially by rises in **interleukins**-6 and -8. It is hypothesised that these events result in activation of polymorphonuclear neutrophils. These activated neutrophils may play an important role in initiating endothelial cell damage leading to the haemodynamic toxicity and the capillary leak syndrome which is typically seen following the administration of **interleukin**-2.

L17 ANSWER 9 OF 20 MEDLINE
ACCESSION NUMBER: 95107729 MEDLINE
DOCUMENT NUMBER: 95107729
TITLE: Dexamethasone treatment of infants at risk for chronic lung disease: surfactant components and inflammatory parameters in airway specimens.
AUTHOR: Kari M A; Raivio K O; Venge P; Hallman M
CORPORATE SOURCE: Children's Hospital, University of Helsinki, Finland..
SOURCE: PEDIATRIC RESEARCH, (1994 Sep) 36 (3) 387-93.
Journal code: OWL. ISSN: 0031-3998.
PUB. COUNTRY: United States
(CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
(MULTICENTER STUDY)
(RANDOMIZED CONTROLLED TRIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199504

AB The mechanisms explaining the beneficial effects of glucocorticoid in ventilator-dependent preterm infants are not known. In the present randomized trial, we evaluated the hypothesis that dexamethasone (DEX) treatment of small, preterm infants at risk for chronic lung disease favorably affects the surfactant system. Twenty-three ventilator-dependent infants, with a mean +/- SD gestational age of 26 +/- 2 wk and a mean birth weight of 836 +/- 173 g, received 1 wk of treatment with either DEX (dose 0.5 mg/kg/d) or placebo beginning at 2 wk of age. The airway specimens were analyzed for surfactant components, surface activity, surfactant inhibitors, and inflammatory mediators. The concentrations of these parameters in epithelial lining fluid were calculated using the urea method. DEX treatment decreased the concentration of nonsedimentable protein in epithelial lining fluid within 3 d ($p < 0.05$). The nonsedimentable fraction of airway specimens decreased the surface activity of surfactant as a function of protein concentration. At a constant protein concentration, the protein from placebo-treated infants inhibited the surface activity of human surfactant in vitro more than protein from DEX-treated infants ($p < 0.05$). DEX transiently increased the concentration of surfactant protein-A in epithelial lining fluid but had

no effect on surface activity of the sedimentable surfactant complex or on concentrations of phosphatidylcholine, IL-1 beta, **lactoferrin**, or myeloperoxidase. We conclude that the acute beneficial effect of DEX treatment in preterm ventilator-dependent infants may in part be mediated through a decrease in the concentration of non-sedimentable protein and a decrease in the capacity of this protein to inhibit surface activity.

L17 ANSWER 10 OF 20 MEDLINE
ACCESSION NUMBER: 92126510 MEDLINE
DOCUMENT NUMBER: 92126510
TITLE: The activation of polymorphonuclear neutrophils and the complement system during immunotherapy with recombinant **interleukin**-2.
AUTHOR: Baars J W; Hack C E; Wagstaff J; Eerenberg-Belmer A J; Wolbink G J; Thijs L G; Strack van Schijndel R J; van der Vall H L; Pinedo H M
CORPORATE SOURCE: Department of Medical Oncology, Free University Hospital, Amsterdam, Netherlands..
SOURCE: BRITISH JOURNAL OF CANCER, (1992 Jan) 65 (1) 96-101. Journal code: AV4. ISSN: 0007-0920.
PUB. COUNTRY: ENGLAND: United Kingdom
(CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199205
AB The toxicity due to **interleukin**-2 (IL-2) strongly resembles the clinical picture seen during septic shock. In septic shock activation of polymorphonuclear neutrophils (PMN) and the complement system contribute significantly to the pathophysiology of the condition. We therefore investigated whether similar events contributed to the toxicity observed with IL-2. Four patients received seven cycles of escalating dose IL-2 (18.0 to 72.0 X 10(6) IU m-2 day-1) and 16 were treated with 20 cycles of fixed dose IL-2 (12.0 or 18.0 X 10(6) IU m-2 day-1). Toxicity, as judged by hypotension (P = less than 0.005) and capillary leakage (fall in serum albumin 18.2 vs 4.0 gm l-1; P = less than 0.0005 and weight gain 4.0 vs 1.2 kg; P = less than 0.025) were worse with the esc. dose protocol. PMN became activated following IL-2 with mean peak elastase/alpha 1-antitrypsin (E alpha 1 A) and **lactoferrin** values of 212 (SEM = 37) and 534 (SEM = 92) ng ml-1 respectively occurring 6 h after the IL-2. Peak values for the esc. dose IL-2 group being generally higher than 500 ng ml-1. Activation of the complement cascade was evidenced by a dose dependent elevation of peak C3a values (fixed dose 9.1 (SEM = 0.6); esc. dose 25.7 (SEM = 6.33); P = less than 0.005) on day 5 of IL-2. There was a significant correlation between C3a levels and the degree of hypotention during the first 24 h after IL-2 (r = 0.91) and parameters of capillary leakage such as weight gain and fall in serum albumin (r = 0.71). These data suggest that activation of PMN initiates endothelial cell damage which subsequently leads to activation of the complement cascade. This latter system then contributes to the haemodynamic changes and capillary leakage seen in IL-2 treated patients.

L17 ANSWER 11 OF 20 MEDLINE
ACCESSION NUMBER: 91077026 MEDLINE
DOCUMENT NUMBER: 91077026
TITLE: New **therapeutic** strategies in the treatment of murine diseases induced by virus and solid tumors: biology and implications for the potential treatment of human leukemia, AIDS, and solid tumors.
AUTHOR: Shen R N; Lu L; Broxmeyer H E
CORPORATE SOURCE: Department of Radiation Oncology/Medicine, Walther Oncology
Center, Indiana School of Medicine, Indianapolis.

SOURCE: CRITICAL REVIEWS IN ONCOLOGY/HEMATOLOGY, (1990) 10 (3) 253-65. Ref: 166
Journal code: AGO. ISSN: 1040-8428.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199104

AB Understanding the biology and treatment of various cancers (including leukemia) and immunodeficiency disorders is still an ongoing and experimental process. Animal models have been and continue to be important to this process. This review will focus in on work by ourselves and others that have used murine models assessing the effects in vivo of the Friend virus complex (FVC, composed of a spleen focus forming virus and a murine leukemia helper virus) and solid tumors with metastatic potential in order to evaluate new and innovative therapies. These therapies include radiation, hyperthermia, and newly recognized naturally occurring biomolecules termed cytokines. These cytokines include, but are not limited to, the interferons, the tumor necrosis factors, the **interleukins**, the hematopoietic colony stimulating factors, **lactoferrin** and E-type prostaglandins. For example, it has been found that **lactoferrin**, when administered early enough, prolongs the survival of mice injected, but not yet infected, with the FVC. Of even greater potential usefulness is that mice already infected with the FVC can be completely rescued from death by treatment with split low dosage (150 cGy) total body irradiation. Irradiation treatment was associated with restoration of the T helper to T suppressor cell ratio, natural killer cell activity and marrow proliferative responses to the mitogens PHA and con A which were compromised by the FVC. More recent studies in our laboratory have demonstrated the potential of the **interleukins** and colony stimulating factors to decrease the metastatic potential of the B16 melanoma and the Lewis Lung Carcinoma cell lines. The cytokines can act in greater than additive fashion and combinations of therapies are possible. This review is meant to increase the awareness of these investigative animal models and the new types of combination therapies that can then be used as the basis for future clinical trials evaluating **therapeutic** efficacy.

L17 ANSWER 12 OF 20 MEDLINE
ACCESSION NUMBER: 90352600 MEDLINE
DOCUMENT NUMBER: 90352600
TITLE: Differentiation and growth modulation of chronic myelogenous leukemia cells by bryostatin.
AUTHOR: Lilly M; Tompkins C; Brown C; Pettit G; Kraft A
CORPORATE SOURCE: Division of Medical Oncology, University of Washington, Seattle.
CONTRACT NUMBER: CA45672 (NCI)
CA42533 (NCI)
CA16049 (NCI)
SOURCE: CANCER RESEARCH, (1990 Sep 1) 50 (17) 5520-5.
Journal code: CNF. ISSN: 0008-5472.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199011

AB We have examined the ability of bryostatin 1 (bryo), an activator of protein kinase C, to induce differentiation of chronic myelogenous

leukemia (CML) cells obtained from peripheral blood. Bryo induced a prompt
and persistent macrophage-like differentiation, as evidenced by functional, morphological, and immunological criteria. Differentiated cells remained viable for at least 21 days with little change in cell number. CML cell cultures treated in semisolid medium with bryo showed diffuse infiltration with single macrophages, as well as discrete macrophage, mixed, and granulocytic colonies. Supernatants of suspension cultures of bryo-treated CML cells contained granulocyte-macrophage colony-stimulating factor (GM-CSF) by enzyme-linked immunosorbent assay. Furthermore, colony formation could be significantly inhibited by the addition of antibodies to GM-CSF. Prolonged liquid culture of CML cells in
bryo reduced colony-forming unit, granulocyte-macrophage content. Bryo-induced differentiation was associated with a decrease in **lactoferrin**, a marker of granulocyte differentiation, and an increase in both c-fms and **interleukin**-1 beta RNA, both of which are expressed by monocytes/macrophages. These data demonstrate that bryostatin 1 is capable of inducing macrophage-like differentiation in maturing CML cells. Furthermore, bryostatin induces secretion of GM-CSF by
such cells in suspension and semisolid medium and also promotes clonal extinction of granulocyte-macrophage progenitors. Bryostatin may be a possible **therapeutic** agent for CML.

L17 ANSWER 13 OF 20 MEDLINE
ACCESSION NUMBER: 86162692 MEDLINE
DOCUMENT NUMBER: 86162692
TITLE: Iron, infection, and neoplasia.
AUTHOR: Weinberg E D
SOURCE: CLINICAL PHYSIOLOGY AND BIOCHEMISTRY, (1986) 4 (1) 50-60.
Ref: 48
Journal code: DHS. ISSN: 0252-1164.
PUB. COUNTRY: Switzerland
Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198607
AB In nearly all forms of life, the number and diversity of enzymes that contain iron or that depend on the presence of this metal for activity are
impressive. Not surprisingly, chemical mechanisms have been evolved by many organisms that permit them to solubilize and acquire iron while at the same time depriving their competitors or their pathogens of this element. Proteins such as transferrin and **lactoferrin** that are employed by vertebrate hosts for iron transport and acquisition can, to some extent, withhold the metal from the siderophores of invading bacteria
and fungi. Attempts also are made by animal hosts to withhold iron from protozoa and neoplastic cells. Unfortunately, pathogenic microorganisms have developed a variety of counter measures that are especially dangerous
in hosts stressed by iron overload in specific fluids, tissues, or cells. In recent years, however, a number of possible methods and agents for strengthening iron-withholding defense have become apparent. Nearly 3,000 papers on various aspects of iron withholding are contained in the 18-year
Medline Database and numerous reviews have been published since 1966. The present paper will focus on developments that have been reported within the past 2 1/2 years.

L17 ANSWER 14 OF 20 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:659489 CAPLUS
DOCUMENT NUMBER: 131:268984

TITLE: Chromatographic purification of human acid .alpha.-glucosidase and its use for treatment of Pompe's disease
INVENTOR(S): Van Corven, Emile; Weggeman, Miranda
PATENT ASSIGNEE(S): Pharming Intellectual Property B.V., Neth.
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9951724	A1	19991014	WO 1999-EP2475	19990406
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9935229	A1	19991025	AU 1999-35229	19990406
PRIORITY APPLN. INFO.:			GB 1998-7464	19980407
			WO 1999-EP2475	19990406

AB The invention provides methods of purifying human acid .alpha.-glucosidase, particularly from the milk of transgenic animals. The methods employ two chromatog. steps. The first step is usually anion exchange chromatog. and the second step is hydrophobic interaction chromatog. The purifn. procedure readily generates human .alpha.-glucosidase in at least 99 % wt./wt. purity. Also provided are **pharmaceutical** compns. and methods for using purified human acid .alpha.-glucosidase in treatment of patients with Pompe's disease.

L17 ANSWER 15 OF 20 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:682302 CAPLUS
DOCUMENT NUMBER: 129:285991
TITLE: Use of **lactoferrin** in the treatment of allergen-induced disorders
INVENTOR(S): Kimber, Ian; Cumberbatch, Marie; Dearman, Rebecca J.; Conneely, Orla M.; Ward, Pauline
PATENT ASSIGNEE(S): Agennix, Inc., USA
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9844940	A1	19981015	WO 1998-US7234	19980410
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9869647	A1	19981030	AU 1998-69647	19980410
EP 979099	A1	20000216	EP 1998-915471	19980410
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, FI
PRIORITY APPLN. INFO.: US 1997-41890 19970410
WO 1998-US7234 19980410

AB The present invention relates to **pharmaceutical** compns. and methods using **lactoferrin** for treating allergic disorders characterized by a local immune response including inflammatory skin reactions, asthma, and arthritis.

L17 ANSWER 16 OF 20 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:324814 CAPLUS
DOCUMENT NUMBER: 129:32288
TITLE: Human **therapeutic** uses of bactericidal/permeability-increasing (BPI) protein products
INVENTOR(S): Friedmann, Nadav; Scannon, Patrick J.; Van Deventer, Sander J. H.; Vonder Mohlen, Marijke A. M.; Wedel, Nancy
PATENT ASSIGNEE(S): XOMA Corp., USA
SOURCE: U.S., 38 pp. Cont.-in-part of U.S. 5,643,875.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5753620	A	19980519	US 1995-378228	19950124
US 5643875	A	19970701	US 1994-291112	19940816
US 5952302	A	19990914	US 1998-81166	19980518
US 5990086	A	19991123	US 1998-203159	19981201
PRIORITY APPLN. INFO.:			US 1994-188221	19940124
			US 1994-291112	19940816
			US 1995-378228	19950124
			US 1996-644287	19960510
			US 1997-927437	19970910

AB Disclosed are methods for treatment of humans exposed to bacterial endotoxin in circulation by administration of bactericidal/permeability-increasing (BPI) protein products. Serol. and hematol. verifiable alleviation of endotoxin-mediated increases in circulating cytokines, fibrinolysis and coagulation factors and changes in lymphocyte counts are obsd. upon such treatment. Also obsd. is alleviation of endotoxin-mediated decreases in systemic vascular resistance index (SVRI) and concomitant increases in cardiac index (CI).

L17 ANSWER 17 OF 20 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:124033 CAPLUS
DOCUMENT NUMBER: 128:162900
TITLE: Treatment and prevention of infections, inflammations and/or tumors with **lactoferrin** and/or lactoferricin
INVENTOR(S): Hanson, Lars A.; Mattsby-Baltzer, Inger; Motas, Cecilia
PATENT ASSIGNEE(S): Holdingbolaget Vid Goteborgs Universitet AB, Swed.; Hanson, Lars A; Mattsby-Baltzer, Inger; Motas, Cecilia
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9806425 A1 19980219 WO 1997-SE1344 19970812
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, CZ, DE, DE, DK, DK, EE, ES, FI, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG
AU 9738727 A1 19980306 AU 1997-38727 19970812
EP 920331 A1 19990609 EP 1997-935939 19970812
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI
PRIORITY APPLN. INFO.: US 1996-23761 19960812
WO 1997-SE1344 19970812

AB The invention relates to a **pharmaceutical** compn. comprising **lactoferrin** and/or lactoferricin for treatment and/or prevention of infections, inflammations, and/or tumors; to the use of **lactoferrin** and lactoferricin in the prodn. of a **pharmaceutical** compn. for treatment and/or prevention of infections, inflammations and tumors; and to a method for treatment and/or prevention of infections, inflammations and/or tumors comprising administration of **lactoferrin** and/or lactoferricin. The invention is particularly well suited for treatment and/or prevention of urinary tract infections and colitis. The **lactoferrin** and/or lactoferricin according to the present invention is preferably orally administered. Furthermore, the compn. comprising **lactoferrin** and/or lactoferricin may be included in an infant formula food.

L17 ANSWER 18 OF 20 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1997:537559 CAPLUS
DOCUMENT NUMBER: 127:156711
TITLE: Human **therapeutic** uses of bactericidal/permeability increasing (BPI) protein products
INVENTOR(S): Friedmann, Nadav; Scannon, Patrick J.; Van Deventer, Sander J. H.; Vonder Mohlen, Marijke A. M.; Wedel, Nancy
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 36 pp. Cont.-in-part of U.S. Ser. No. 188,221, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5643875	A	19970701	US 1994-291112	19940816
CA 2181816	AA	19950727	CA 1995-2181816	19950124
AU 9516944	A1	19950808	AU 1995-16944	19950124
AU 703728	B2	19990401		
EP 741575	A1	19961113	EP 1995-908723	19950124
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
CN 1145033	A	19970312	CN 1995-191325	19950124
JP 09508130	T2	19970819	JP 1995-519768	19950124
US 5753620	A	19980519	US 1995-378228	19950124
US 5952302	A	19990914	US 1998-81166	19980518
US 5990086	A	19991123	US 1998-203159	19981201
PRIORITY APPLN. INFO.:			US 1994-188221	19940124
			US 1994-291112	19940816

US 1995-378228 19950124
WO 1995-US1151 19950124
US 1996-644287 19960510
US 1997-927437 19970910

AB Disclosed are methods for treatment of humans exposed to bacterial endotoxin in circulation by administration of bactericidal/permeability-increasing (BPI) protein products. Serol. and hematol. verifiable alleviation of endotoxin-mediated increases in circulating cytokines, fibrinolysis and coagulation factors and changes in lymphocyte counts are obsd. upon such treatment. Also obsd. is alleviation of endotoxin-mediated decreases in systemic vascular resistance index (SVRI) and concomitant increases in cardiac index (CI).

L17 ANSWER 19 OF 20 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1996:612679 CAPLUS
DOCUMENT NUMBER: 125:230803
TITLE: **Pharmaceutical** and cosmetic compositions containing histamine and **interleukin** and .alpha.-tumor necrosis factor antagonists
INVENTOR(S): De Lacharriere, Olivier; Breton, Lionel; Cohen, Catherine
PATENT ASSIGNEE(S): Oreal S. A., Fr.
SOURCE: Can. Pat. Appl., 25 pp.
CODEN: CPXXEB
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 2166179	AA	19960629	CA 1995-2166179	19951227
FR 2728793	A1	19960705	FR 1994-15796	19941228
FR 2728793	B1	19970207		
EP 729750	A1	19960904	EP 1995-402677	19951128
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08231432	A2	19960910	JP 1995-341294	19951227
US 5658581	A	19970819	US 1995-580291	19951228
US 5993833	A	19991130	US 1997-879889	19970620
PRIORITY APPLN. INFO.:			FR 1994-15796	19941228
			US 1995-580291	19951228

AB The title compns. are disclosed. A lotion contained cetrizine 0.001, antioxidants 0.05, isopropanol 40.00, preservatives 0.30, and water q.s. 100%.

L17 ANSWER 20 OF 20 BIOSIS COPYRIGHT 2000 BIOSIS
ACCESSION NUMBER: 1999:315256 BIOSIS
DOCUMENT NUMBER: PREV199900315256
TITLE: Is major liver surgery associated with an increased systemic inflammatory response? A prospective comparison of hemihepatectomy and other major abdominal surgery.
AUTHOR(S): Wiezer, Marinus J. (1); Meijer, Catharina; Vuylsteke, Ronald; Pullens, Renee H.; Prins, Hubert A.; Cuesta, Miguel A.; Meijer, Sybren; Hack, C. Erik; van Leeuwen, Paul A.M. (1)
CORPORATE SOURCE: (1) Department of Surgery, Free University Hospital, De Boelelaan 1117, 1081 HV, Amsterdam Netherlands
SOURCE: Liver, (June, 1999) Vol. 19, No. 3, pp. 220-227.
ISSN: 0106-9543.
DOCUMENT TYPE: Article
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Aims/Background: Extensive liver resection is associated with a higher morbidity and mortality than other major abdominal surgery. Because the liver is responsible for the clearance of pathogenic particles as well as the clearance and degradation of several inflammatory mediators, the high rate of complications after liver surgery may be due to an enhanced or prolonged inflammatory response. The objective of this prospective study was to investigate whether major liver resection is associated with an enhanced systemic inflammatory response. Methods: The course of various inflammatory parameters was studied in 12 patients undergoing a hemihepatectomy and the results were compared with those of 12 patients undergoing other major abdominal surgery. Results: After hemihepatectomy, the plasma levels of IL-6, IL-8, sPLA2 and elastase were similar to the levels after other major abdominal surgery, though the hepatectomized patients showed higher levels of **lactoferrin**, possibly due to impaired hepatic clearance. In addition, the hemihepatectomized patients showed signs of impaired liver function, as was indicated by increased plasma bilirubin and ASAT levels, whereas the other patients did not. Conclusions: The inflammatory response associated with major liver resection is not significantly different from that after other major abdominal surgery, and therefore does not explain the increased complication rate that is seen after major liver resection. We infer that the most important factor in the development of complications after liver resection may be the hepatic failure itself.

```
=> s interleukin (w) - (w) 1?

   1 FILES SEARCHED...
TERM '1?' EXCEEDED TRUNCATION LIMITS - SEARCH ENDED
   2 FILES SEARCHED...
TERM '1?' EXCEEDED TRUNCATION LIMITS - SEARCH ENDED

<------User Break------>
u
SEARCH ENDED BY USER
L18           0 INTERLEUKIN (W) - (W) 1?
You have entered a truncated stem which occurs in too many terms.
Make the stem longer and try again.  For example, if your original
term was 'degr?' to search for variations and the abbreviation for
'degradation', you could replace it with the expression '(degrdn OR
degrad?)'.  If your search term was numeric, e.g., 'C>5', reduce the
size of the range.

=> log y

COST IN U.S. DOLLARS                                SINCE FILE      TOTAL
                                                       ENTRY    SESSION
FULL ESTIMATED COST                                   105.74     161.53

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)          SINCE FILE      TOTAL
                                                       ENTRY    SESSION
CA SUBSCRIBER PRICE                                    -5.01      -5.01

STN INTERNATIONAL LOGOFF AT 15:57:59 ON 22 FEB 2000
```